

## Bioaerosols and the scientific method

### BIOAEROSOLS

Aerosols are small particles suspended in air, and bioaerosols are those derived from living organisms. The living components of the aerosol are designed to reproduce their species so that pollen joins other particles in the aerosol to be transported to the appropriate host plant. Likewise, fungi release spores that are transported in the ambient aerosol to land eventually in an environment suitable for their growth.

Bioaerosols are ubiquitous and have always been a part of our everyday life. It may be that some respiratory exposure to fungi is necessary for the development of a healthy immune system. Why then has so much panic arisen concerning fungal spore exposure? At least in part, the answer to this question lies in how we and others interpret observational data and how we communicate our interpretations.

The public relies primarily on television for "facts," generally believing most of what they hear. The media may or may not take care over interpretations but are inevitably forced to spin information in ways that promote their particular newspaper or television show. Physicians are also influenced by the media and by the opinions of their patients. In addition, they read the published literature, often reading only abstracts and conclusions, and generally accepting conclusions as presented when the field is outside their primary experience. Environmental investigators are similarly driven by the media, by their clients, and by the fact that unpopular results or expensive protocols do not support business.

Scientists are supposedly driven only by the truth. Objectivity is the goal in all scientific investigations. Thus, controls are a part of studies, blinding to treatment protocols is used, and so forth. However, scientists also read the newspapers and watch television and can be "educated" into biased positions. Bias is the single most important problem that faces most scientists. Unfortunately, no one is completely unbiased, and it becomes easy to design experiments or studies that attempt to *prove* a particular hypothesis rather than actually *testing whether or not* the hypothesis is true. Many of the studies on mold-related illness in homes and buildings suffer from bias: they were designed to prove a specific hypothesis either purposely or, more often, due to the unrecognized bias of the investigator.

### HYPOTHESIS TESTING

It is helpful to recall the elements of hypothesis testing to be able to judge whether or not conclusions in a journal article, a newspaper, or a television show are justified.

The first step is to develop an idea or make an observation. Perhaps an occupant of a house complains of joint pains when in her home and feels better outside or in other buildings. She has heard about toxic mold and is afraid this might be her problem.

The next step is to ask a specific question that can be answered using the methods at hand and then formulate the question as a statement. In the joint pain case, the question could be, "Is toxic mold causing this person's symptoms?" The statement or hypothesis then becomes, "Toxic mold is causing the symptoms." The null hypothesis (ie, the hypothesis to be tested) is, "Toxic mold is not causing the symptoms."

Now a protocol can be developed to test the probability that the null hypothesis is correct (ie, your original hypothesis is wrong). To avoid bias it is always best to state your most probable hypothesis then to try to prove it wrong. The protocol, then, should take into account as many other potential causes for the symptoms as possible, and well designed controls should be a major emphasis. Thus, in the joint pain case, one would try as intensively as possible to prove that no exposure to toxic mold occurred or that the symptoms are easily explained by some other factor. If you cannot document any other cause for the illness, you have documented that the symptoms could be related to some specific mold toxin, you have documented exposure to the toxin, as well as documented that everyone exposed has similar symptoms, then you may conclude with some measurable probability that your hypothesis is correct.

### PROBABILITY

There are no absolutes. For every study or hypothesis you are testing you have to decide in advance the percentage of time that you can afford to be wrong. Scientists usually insist on a less than 5% or, more often, a less than 1% chance that they are wrong. Experimental protocols are then designed so that these stringent requirements for error are met.

For physicians, acceptability depends on the impact of the error. Unfortunately, there appears to be little negative impact if a physician says to a patient that mold is causing symptoms, even though the physician does not know whether or not the patient has any exposure to toxic mold. Equally unfortunate, there is a huge negative impact if the patient spends his/her life savings trying to get rid of nonexistent mold or if the symptoms turn out to be part of a completely different serious illness.

## KINDS OF EVIDENCE FOR HEALTH EFFECTS

The evidence for mold-associated disease falls into 4 general categories: anecdotal evidence, case studies, epidemiologic studies, and experimental evidence.

Anecdotal reports are by far the most common for mold-related illness. A person will begin to suspect that mold is causing a problem and will communicate this feeling to others or will bring the fears to a physician. Often, a mold investigator will have collected some samples and told the person there is mold in the house. The physician may then, in the absence of any other clear diagnosis, say that the mold may be causing the problem. The patient interprets this as "the mold is making me sick." Often these cases occur in homes where mold levels are normal given the type of ventilation, the season of the year, and the probability that the mold connection is real is less than 50%. The cases reported in the media are anecdotal and cannot be used as reliable evidence of a cause and effect. This includes many of the incidents where houses have been destroyed because of the presence of "toxic mold." Patient reports to physicians are also anecdotal. These may or may not be reliable, and it is up to the physician to develop an appropriate diagnosis. Again, these cases do not constitute proof of a cause/effect relationship unless the case is studied further. A large number of anecdotal reports may lead to well designed studies that either confirm or refute the cause/effect relationship.

Case studies range from one step up from anecdotal to reasonably well documented observational studies of one case or a small cluster of cases. Although the data were analyzed and reported epidemiologically, the reports of cases of hemosiderosis in Cleveland infants are actually case studies. A well done case study can provide excellent clues as to potential causes for illness. A poorly done study can lead to misinterpretation and inappropriate extrapolation to other situations. Even well done case studies can be misinterpreted. An example here is the study by Croft et al<sup>1</sup> of a *Stachybotrys*-contaminated home where one occupant was complaining of time distortion and other central nervous system effects. Although the case study was very well done and the conclusions were carefully stated, this study has been extrapolated to endless cases where dizziness, fatigue, and nausea were blamed on *Stachybotrys*.

As case studies, the Cleveland infant cases<sup>2</sup> were also well documented and reported and, at least initially, the conclusions were carefully stated. However, subsequent studies have focused so intensely on *Stachybotrys* that objectivity appears to have been lost and other potential causes for the outbreak of illness may have been overlooked.

No well designed epidemiologic studies have documented a relationship between fungal exposure and any specific toxicosis in nonagricultural environments. The good epidemiologic studies have focused on dampness and mold exposure and its relationship to lower respiratory illness in children.<sup>3,4</sup> Also, several studies have now documented the case for allergy, asthma, and fungal exposure.<sup>5,6</sup>

Experimental evidence abounds on the effects of isolated fungal toxins and changes in the lung.<sup>7-9</sup> Clearly, if a rat or mouse lung (or a human lung) is exposed to sufficient toxin, changes occur that could lead to bleeding. However, the doses required appear to be much higher than are likely even in relatively moldy houses. No experimental evidence supports a role for the *Stachybotrys* toxins in central nervous system illnesses, although this is usually the type of symptoms reported in conjunction with suspected mold contamination.

## WHAT TO DO?

### *The Journal Literature*

Authors need to ask associates to review papers specifically for study design and accuracy of conclusions.

Reviewers also need to address these topics and need to address problems with either study design or conclusions specifically in writing.

Editorial boards must not be swayed by the fame of an author but must carefully consider comments related to study design and conclusions. Papers in which conclusions are not justified by the data presented should not be published.

Readers need to evaluate the editorial policy of the journals they read. Even with good journals, each reader is responsible for evaluating the quality of the reported research if any action is to be taken based on the conclusions presented by the authors.

### *Education*

Everyone involved in mold-related problems needs to be properly educated in the nature of the fungi, where and how they grow, how exposure occurs, and in the state of the information on health effects. Clear and interesting information presented on Web sites such as that of the American College of Allergy, Asthma, and Immunology would be a good start. Popular books on the topic need to be written by thoughtful experts.

### *Research*

Research continues to be important. At present, no broad epidemiologic studies have been reported that evaluate objective evidence of toxicosis in people living in moldy homes or working in moldy office buildings. No coordinated clinical study of people reporting mold-related illness has been conducted, including ones that focus on other possible causes for the reported symptoms. Although a lot of experimental data are available, none report consequences of low-level long-term exposure. We still do not know the actual size of particles on which mold toxins are carried. Finally, we know nothing about synergistic effects among the components of indoor aerosols. This last part is extremely important, since it is likely that smoking played some role in the Cleveland infant cluster of disease.<sup>2</sup>

The article in this issue by Chapman et al<sup>10</sup> is a start at educating us on the complexity of fungi, fungal exposure, and the extent of evidence for particular disease states. The med-

ical community still has a great deal of work to do if the mold panic is to be abated so that we can focus on the science of fungal-related disease.

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